

## WEST Search History

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DATE: Friday, February 09, 2007

Hide?	Set Name	Query	Hit Count
DB=PGPB,USPT; PLUR=YES; OP=OR			
<input type="checkbox"/>	L8	L6 and pet\$5.clm.	1
<input type="checkbox"/>	L7	L6 and saxena.in.	2
<input type="checkbox"/>	L6	((rnase\$4 or ribonucleas\$4) same pipien\$4) and (gene\$4 or cdna\$4 or dna\$4 or mrna\$4 or polynucleotid\$4 or nucleic\$4).clm.	29
DB=PGPB,USPT,EPAB,JPAB,DWPI; PLUR=YES; OP=OR			
<input type="checkbox"/>	L5	l1 and saxena.in.	2
<input type="checkbox"/>	L4	L3 same (isolat\$\$ or clon\$4 or characteri\$4 or recombinan\$4 or purif\$4 or express\$4)	20
<input type="checkbox"/>	L3	L1 same (gene\$4 or cdna\$4 or dna\$4 or mrna\$4 or polynucleotid\$4 or nucleic\$4)	23
<input type="checkbox"/>	L2	L1 same tumo\$4	36
<input type="checkbox"/>	L1	(rnase\$4 or ribonucleas\$4) same pipien\$4	47

END OF SEARCH HISTORY

=> d his full

(FILE 'HOME' ENTERED AT 12:20:26 ON 09 FEB 2007)

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE, AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS, CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 12:20:43 ON 09 FEB 2007  
SEA (RNAS? OR RIBONUCLEAS?)(S)PIPIEN?

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1 FILE ADISCTI  
5 FILE AQUASCI  
2 FILE BIOENG  
29 FILE BIOSIS  
5 FILE BIOTECHABS  
5 FILE BIOTECHDS  
10 FILE BIOTECHNO  
2 FILE CABA  
36 FILE CAPLUS  
1 FILE CIN  
4 FILE DDFU  
90 FILE DGENE  
2 FILE DISSABS  
6 FILE DRUGU  
17 FILE EMBASE  
16 FILE ES BIOBASE  
12 FILE GENBANK  
6 FILE IFIPAT  
6 FILE IMSDRUGNEWS  
1 FILE IMSRESEARCH  
16 FILE LIFESCI  
19 FILE MEDLINE  
5 FILE PASCAL  
3 FILE PHAR  
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2 FILE PHIN  
10 FILE PROMT  
1 FILE PROUSDDR  
20 FILE SCISEARCH  
33 FILE TOXCENTER  
39 FILE USPATFULL  
4 FILE USPAT2  
5 FILE WPIDS  
5 FILE WPINDEX  
6 FILE NLDB

L1 QUE (RNAS? OR RIBONUCLEAS?)(S) PIPIEN?

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D RANK

FILE 'USPATFULL, CAPLUS, TOXCENTER, BIOSIS, SCISEARCH, MEDLINE, EMBASE, ES BIOBASE, LIFESCI, GENBANK' ENTERED AT 12:22:17 ON 09 FEB 2007

L2 237 SEA (RNAS? OR RIBONUCLEAS?)(S) PIPIEN?  
L3 193 SEA L2 (S)(GENE? OR DNA? OR RNA? OR MRNA? OR CDNA? OR POLYNUCLEOTI? OR NUCLEIC?)  
L4 126 SEA L3 (S)(ISOLAT? OR CLON? OR CHARACTER? OR PURIF? OR EXPRESS? OR RECOMBINAN?)  
L5 61 DUP REM L4 (65 DUPLICATES REMOVED)  
D TI L5 1-64  
D IBIB ABS L5 1 2 5 13 16 28 30 31 32 37 40 44 47 48 53

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Welcome to STN International! Enter x:x

LOGINID:sssptal652dmr

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TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS	4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS	5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS	6	NOV 10	CA/CAPLUS F-Term thesaurus enhanced
NEWS	7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS	8	NOV 20	CA/CAPLUS to MARPAT accession number crossover limit increased to 50,000
NEWS	9	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS	10	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS	11	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS	12	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS	13	DEC 18	CA/CAPLUS pre-1967 chemical substance index entries enhanced with preparation role
NEWS	14	DEC 18	CA/CAPLUS patent kind codes updated
NEWS	15	DEC 18	MARPAT to CA/CAPLUS accession number crossover limit increased to 50,000
NEWS	16	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS	17	DEC 27	CA/CAPLUS enhanced with more pre-1907 records
NEWS	18	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS	19	JAN 16	CA/CAPLUS Company Name Thesaurus enhanced and reloaded
NEWS	20	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS	21	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS	22	JAN 22	CA/CAPLUS updated with revised CAS roles
NEWS	23	JAN 22	CA/CAPLUS enhanced with patent applications from India
NEWS	24	JAN 29	PHAR reloaded with new search and display fields
NEWS	25	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS EXPRESS	NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.		
NEWS HOURS	STN Operating Hours Plus Help Desk Availability		
NEWS LOGIN	Welcome Banner and News Items		
NEWS IPC8	For general information regarding STN implementation of IPC 8		
NEWS X25	X.25 communication option no longer available		

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FILE 'HOME' ENTERED AT 12:20:26 ON 09 FEB 2007

=> index bioscience medicine

FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.21	0.21

FULL ESTIMATED COST

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE, AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS, CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 12:20:43 ON 09 FEB 2007

71 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view search error messages that display as 0\* with SET DETAIL OFF.

=> s (rnas? or ribonucleas?) (s)pipien?

- 1 FILE ADISCTI
- 5 FILE AQUASCI
- 2 FILE BIOENG
- 29 FILE BIOSIS
- 5 FILE BIOTECHABS
- 5 FILE BIOTECHDS
- 10 FILE BIOTECHNO
- 2 FILE CABA
- 36 FILE CAPLUS
- 1 FILE CIN
- 4 FILE DDFU
- 90 FILE DGENE
- 2 FILE DISSABS

25 FILES SEARCHED...

- 6 FILE DRUGU
- 17 FILE EMBASE
- 16 FILE ESBIODBASE
- 12 FILE GENBANK
- 6 FILE IFIPAT
- 6 FILE IMSDRUGNEWS
- 1 FILE IMSRESEARCH
- 16 FILE LIFESCI
- 19 FILE MEDLINE
- 5 FILE PASCAL
- 3 FILE PHAR
- 1 FILE PHARMAML
- 2 FILE PHIN
- 10 FILE PROMT
- 1 FILE PROUSDDR
- 20 FILE SCISEARCH
- 33 FILE TOXCENTER
- 39 FILE USPATFULL

61 FILES SEARCHED...

- 4 FILE USPAT2
- 5 FILE WPIDS
- 5 FILE WPINDEX
- 6 FILE NLDB

35 FILES HAVE ONE OR MORE ANSWERS, 71 FILES SEARCHED IN STNINDEX

L1 QUE (RNAS? OR RIBONUCLEAS?) (S) PIPIEN?

=> d rank

F1	90	DGENE
F2	39	USPATFULL
F3	36	CAPLUS
F4	33	TOXCENTER
F5	29	BIOSIS
F6	20	SCISEARCH
F7	19	MEDLINE
F8	17	EMBASE
F9	16	ESBIOBASE
F10	16	LIFESCI
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F15	6	IFIPAT
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F18	5	AQUASCI
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F22	5	WPIDS
F23	5	WPINDEX
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F26	3	PHAR
F27	2	BIOENG
F28	2	CABA
F29	2	DISSABS
F30	2	PHIN
F31	1	ADISCTI
F32	1	CIN
F33	1	IMSRESEARCH
F34	1	PHARMAML
F35	1	PROUSDDR

=> file f2-f11

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.89	2.10

FILE 'USPATFULL' ENTERED AT 12:22:17 ON 09 FEB 2007  
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FILE 'CAPLUS' ENTERED AT 12:22:17 ON 09 FEB 2007  
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FILE 'ESBIOBASE' ENTERED AT 12:22:17 ON 09 FEB 2007  
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FILE 'LIFESCI' ENTERED AT 12:22:17 ON 09 FEB 2007  
COPYRIGHT (C) 2007 Cambridge Scientific Abstracts (CSA)

FILE 'GENBANK' ENTERED AT 12:22:17 ON 09 FEB 2007

```
=> s (rnas? or ribonucleas?)(s)piapien?
L2      237 (RNAS? OR RIBONUCLEAS?)(S) PIPIEN?

=> s l2 (s)(gene? or dna? or rna? or mrna? or cdna? or polynucleoti? or nucleic?)
  2 FILES SEARCHED...
  7 FILES SEARCHED...
  8 FILES SEARCHED...
L3      193 L2 (S)(GENE? OR DNA? OR RNA? OR MRNA? OR CDNA? OR POLYNUCLEOTI?
      OR NUCLEIC?)

=> s l3 (s)(isolat? or clon? or character? or purif? or express? or recombinan?)
  6 FILES SEARCHED...
  8 FILES SEARCHED...
L4      126 L3 (S)(ISOLAT? OR CLON? OR CHARACTER? OR PURIF? OR EXPRESS? OR
      RECOMBINAN?)
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=> dup rem l4
DUPLICATE IS NOT AVAILABLE IN 'GENBANK'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L4
L5      61 DUP REM L4 (65 DUPLICATES REMOVED)
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=> d ti l5 1-64
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L5      ANSWER 1 OF 61  USPATFULL on STN
TI      Cytotoxic ribonuclease variants

L5      ANSWER 2 OF 61  USPATFULL on STN
TI      Cytotoxic ribonuclease variants

L5      ANSWER 3 OF 61  USPATFULL on STN
TI      Biological materials and uses thereof

L5      ANSWER 4 OF 61  USPATFULL on STN
TI      Methods for reduced renal uptake of protein conjugates

L5      ANSWER 5 OF 61  USPATFULL on STN
TI      Fusion proteins containing recombinant cytotoxic RNases

L5      ANSWER 6 OF 61  USPATFULL on STN
TI      Methods of and compositions for inhibiting the proliferation of
      mammalian cells

L5      ANSWER 7 OF 61  USPATFULL on STN
TI      Folate conjugates and complexes

L5      ANSWER 8 OF 61  USPATFULL on STN
TI      Immunotoxins directed against malignant cells

L5      ANSWER 9 OF 61  USPATFULL on STN
TI      Removal of N-terminal methionine from proteins by engineered methionine
      aminopeptidase

L5      ANSWER 10 OF 61 USPATFULL on STN
TI      Non-antigenic toxin-conjugate and fusion protein of internalizing
      receptor system
```

L5 ANSWER 11 OF 61 USPATFULL on STN  
 TI Methods of and compositions for inhibiting the proliferation of mammalian cells

L5 ANSWER 12 OF 61 USPATFULL on STN  
 TI Albumin fusion proteins

L5 ANSWER 13 OF 61 USPATFULL on STN  
 TI Recombinant anti-tumor RNase

L5 ANSWER 14 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN  
 TI Recombinant production in mammalian cells of immunotoxins containing cytotoxic ribonuclease, such as ranpirnase, fused to an immunoglobulin, and therapeutic uses

L5 ANSWER 15 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1  
 TI Efficient killing of CD22+ tumor cells by a humanized diabody-RNase fusion protein

L5 ANSWER 16 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2  
 TI Status of RNAs, localized in *Xenopus laevis* oocytes, in the frogs *Rana pipiens* and *Eleutherodactylus coqui*

L5 ANSWER 17 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3  
 TI Recombinant autocyclized and cysteinized ranpirnase containing cleavable PelB leader peptide and Met23→L and Ser72→Cys mutations, its cDNA and expression vector, and methods of making them

L5 ANSWER 18 OF 61 USPATFULL on STN  
 TI Antibody/receptor targeting moiety for enhanced delivery of armed ligand

L5 ANSWER 19 OF 61 USPATFULL on STN  
 TI Antibody/receptor targeting moiety for enhanced delivery of armed ligand

L5 ANSWER 20 OF 61 Elsevier BIOBASE COPYRIGHT 2007 Elsevier Science B.V. on STN  
 TI trans-Packaged west nile virus-like particles: Infectious properties in vitro and in infected mosquito vectors

L5 ANSWER 21 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 5  
 TI Removal of N-terminal methionine from recombinant proteins by engineered *E. coli* methionine aminopeptidase

L5 ANSWER 22 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 6  
 TI Treatment of Jurkat acute T-lymphocytic leukemia cells by onconase (Ranpirnase) is accompanied by an altered nucleocytoplasmic distribution and reduced expression of transcription factor NF- $\kappa$ B

L5 ANSWER 23 OF 61 Elsevier BIOBASE COPYRIGHT 2007 Elsevier Science B.V. on STN  
 TI Quantitative analysis, using MALDI-TOF mass spectrometry, of the N-terminal hydrolysis and cyclization reactions of the activation process of onconase

L5 ANSWER 24 OF 61 USPATFULL on STN  
 TI Albumin fusion proteins

L5 ANSWER 25 OF 61 USPATFULL on STN  
 TI Methods for reduced renal uptake of protein conjugates

L5 ANSWER 26 OF 61 USPATFULL on STN  
 TI Immunoconjugates of toxins directed against malignant cells

L5 ANSWER 27 OF 61 USPATFULL on STN

TI Immunotoxins directed against malignant cells  
 L5 ANSWER 28 OF 61 USPATFULL on STN  
 TI Recombinant onconase and chemical conjugates and fusion proteins of recombinant onconase  
 L5 ANSWER 29 OF 61 USPATFULL on STN  
 TI Non-antigenic toxin-conjugate and fusion protein of internalizing receptor system  
 L5 ANSWER 30 OF 61 USPATFULL on STN  
 TI Recombinant anti-tumor RNase  
 L5 ANSWER 31 OF 61 USPATFULL on STN  
 TI Mutant form of cytotoxic ribonucleolytic protein which allows production by recombinant methods  
 L5 ANSWER 32 OF 61 USPATFULL on STN  
 TI Mutant form of a cytotoxic ribonucleolytic protein which allows production by recombinant methods  
 L5 ANSWER 33 OF 61 Elsevier BIOBASE COPYRIGHT 2007 Elsevier Science B.V. on STN DUPLICATE  
 TI The structural integrity exerted by N-terminal pyroglutamate is crucial for the cytotoxicity of frog ribonuclease from Rana pipiens  
 L5 ANSWER 34 OF 61 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN  
 TI Treatment of human Daudi lymphoma with anti-MUC1 antibody-targeted RNase in SCID mice.  
 L5 ANSWER 35 OF 61 USPATFULL on STN  
 TI Immunotoxins, comprising an internalizing antibody, directed against malignant and normal cells  
 L5 ANSWER 36 OF 61 USPATFULL on STN  
 TI METHODS FOR REDUCED RENAL UPTAKE OF PROTEIN CONJUGATES  
 L5 ANSWER 37 OF 61 USPATFULL on STN  
 TI Methods of making nucleic acids encoding ribonucleases  
 L5 ANSWER 38 OF 61 USPATFULL on STN  
 TI Method of treatment with a non-antigenic toxin-conjugate and fusion protein of internalizing receptor system  
 L5 ANSWER 39 OF 61 USPATFULL on STN  
 TI Immunotoxins directed against malignant cells  
 L5 ANSWER 40 OF 61 USPATFULL on STN  
 TI Nucleic acids encoding ribonucleases and methods of making them  
 L5 ANSWER 41 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 8  
 TI Mechanism of ribonuclease cytotoxicity  
 L5 ANSWER 42 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 9  
 TI Rapid Diversification of RNase A Superfamily Ribonucleases from the Bullfrog, Rana catesbeiana  
 L5 ANSWER 43 OF 61 TOXCENTER COPYRIGHT 2007 ACS on STN  
 TI Mechanism of ribonuclease cytotoxicity  
 L5 ANSWER 44 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 10  
 TI Purification and sequences of RNase-like glycoproteins from Rana pipiens and their use in the treatment of tumors



L5 ANSWER 45 OF 61 USPATFULL on STN  
 TI Non-antigenic toxin-conjugate and fusion protein of internalizing receptor system

L5 ANSWER 46 OF 61 USPATFULL on STN  
 TI Recombinant ribonuclease proteins

L5 ANSWER 47 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 11  
 TI A gender-specific mRNA encoding a cytotoxic ribonuclease contains a 3' UTR of unusual length and structure

L5 ANSWER 48 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 12  
 TI Recombinant anti-tumor RNase

L5 ANSWER 49 OF 61 USPATFULL on STN  
 TI Selective RNase cytotoxic reagents

L5 ANSWER 50 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 13  
 TI Onconase immunotoxins directed against malignant B-cells

L5 ANSWER 51 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 14  
 TI The solution structure of a cytotoxic ribonuclease from the oocytes of *Rana catesbeiana* (bullfrog)

L5 ANSWER 52 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 15  
 TI Amino acid-substituted analogs of the cytostatic, cytotoxic ribonuclease Onconase that can be manufactured on a large scale

L5 ANSWER 53 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN  
 TI Recombinant ribonuclease proteins and their use for killing tumor cells

L5 ANSWER 54 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN  
 TI Expression and characterization of a cytotoxic human-frog chimeric ribonuclease: potential for cancer therapy

L5 ANSWER 55 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 16  
 TI Anti-tumor ribonuclease, combined with or conjugated to monoclonal antibody MRK16, overcomes multidrug resistance to vincristine in vitro and in vivo

L5 ANSWER 56 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 17  
 TI Enhancement of vincristine cytotoxicity in drug-resistant cells by simultaneous treatment with onconase, an antitumor ribonuclease

L5 ANSWER 57 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 18  
 TI Toxicity of an antitumor ribonuclease to Purkinje neurons

L5 ANSWER 58 OF 61 LIFESCI COPYRIGHT 2007 CSA on STN  
 TI A cytotoxic ribonuclease: Study of the mechanism of onconase cytotoxicity.

L5 ANSWER 59 OF 61 LIFESCI COPYRIGHT 2007 CSA on STN  
 TI Cytotoxic onconase and ribonuclease A chimeras: Comparison and in vitro characterization.

L5 ANSWER 60 OF 61 LIFESCI COPYRIGHT 2007 CSA on STN  
 TI Sequence and expression of a frog brain complementary DNA encoding a kainate-binding protein.

L5 ANSWER 61 OF 61 GENBANK® COPYRIGHT 2007 on STN

TITLE (TI): Recombinant anti-tumor rnase

=> d ibib abs 15 1 2 5 13 16 28 30 31 32 37 40 44 47 48 53

L5 ANSWER 1 OF 61 USPATFULL on STN

ACCESSION NUMBER: 2007:4344 USPATFULL  
TITLE: Cytotoxic ribonuclease variants  
INVENTOR(S): Raines, Ronald T., Madison, WI, UNITED STATES  
Mitchell, Julie C., Madison, WI, UNITED STATES  
Rutkoski, Thomas J., Madison, WI, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2007003537	A1	20070104
APPLICATION INFO.:	US 2006-454379	A1	20060616 (11)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2005-690970P	20050616 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	QUARLES & BRADY LLP, FIRSTAR PLAZA, ONE SOUTH PINCKNEY STREET, P.O. BOX 2113 SUITE 600, MADISON, WI, 53701-2113, US	

NUMBER OF CLAIMS: 11  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 3 Drawing Page(s)  
LINE COUNT: 818

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to altered forms of members of the RNase A superfamily. An RNase A can be modified to be cytotoxic by altering its amino acid sequence so that it is not bound easily by the ribonuclease inhibitor while still retaining catalytic properties. While earlier work had identified some modifications to RNase A that would result in cytotoxicity, the use of the FADE algorithm for molecular interaction analysis has led to several other locations that were candidates for modification. Some of those modifications did result in RNase A variants with increase cytotoxicity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 2 OF 61 USPATFULL on STN

ACCESSION NUMBER: 2006:340357 USPATFULL  
TITLE: Cytotoxic ribonuclease variants  
INVENTOR(S): Raines, Ronald T., Madison, WI, UNITED STATES  
Phillips, George N. JR., Madison, WI, UNITED STATES  
Johnson, R. Jeremy, Middleton, WI, UNITED STATES  
McCoy, Jason G., Madison, WI, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2006292137	A1	20061228
APPLICATION INFO.:	US 2006-454418	A1	20060616 (11)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2005-691311P	20050616 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	QUARLES & BRADY LLP, FIRSTAR PLAZA, ONE SOUTH PINCKNEY STREET, P.O. BOX 2113 SUITE 600, MADISON, WI, 53701-2113, US	

NUMBER OF CLAIMS: 23  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 5 Drawing Page(s)  
LINE COUNT: 1560

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to cytotoxic variants of human ribonuclease 1 (RNase 1) identified through analysis of the interaction between RNase 1

and the human ribonuclease inhibitor (hRI) as defined by the three dimensional (3-D) atomic structure of the RNase 1 hRI complex. Also disclosed is the 3-D structure of the hRI.RNase 1 complex and methods for designing the RNase 1 variants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 5 OF 61 USPATFULL on STN

ACCESSION NUMBER: 2006:15863 USPATFULL  
TITLE: Fusion proteins containing recombinant cytotoxic RNases  
INVENTOR(S): Goldenberg, David M., Mendham, NJ, UNITED STATES  
Hansen, Hans J., Picayune, MS, UNITED STATES  
Chang, Chien-Hsing, Downingtown, PA, UNITED STATES  
Vanama, Sailaja, Morristown, NJ, UNITED STATES  
Rossi, Edmund A., Nutley, NJ, UNITED STATES  
PATENT ASSIGNEE(S): Immunomedics, Inc., Morris Plains, NJ, UNITED STATES  
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2006014245	A1	20060119
APPLICATION INFO.:	US 2005-56182	A1	20050214 (11)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2004-544227P	20040213 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Heller Ehrman White & McAuliffe, Suite 300, 1666 K Street, N.W., Washington, DC, 20006, US	
NUMBER OF CLAIMS:	40	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	14 Drawing Page(s)	
LINE COUNT:	1524	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Recombinant immunotoxins containing a cytotoxic RNase fused to an antibody or antibody fragment may be produced in mammalian cell culture. Surprisingly, immunotoxins containing a cytotoxic RNase fused to the N-terminus of one antibody variable domain can be prepared and retain the ability to specifically bind antigen. The immunotoxins may be used in a variety of therapeutic methods for treating diseases or syndromes associated with unwanted or inappropriate cell proliferation or activation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 13 OF 61 USPATFULL on STN

ACCESSION NUMBER: 2005:71048 USPATFULL  
TITLE: Recombinant anti-tumor RNase  
INVENTOR(S): Rybak, Susanna M., Frederick, MD, United States  
Newton, Dianne L., Rockville, MD, United States  
PATENT ASSIGNEE(S): The United States of America as represented by the Secretary of the Department of Health and Human Services, Washington, DC, United States (U.S. government)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6869604	B1	20050322
	WO 9950398		19991007
APPLICATION INFO.:	US 2001-622613		20010731 (9)
	WO 1999-US6641		19990326
			20010731 PCT 371 date

NUMBER	DATE
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PRIORITY INFORMATION: US 1998-79751P 19980327 (60)  
DOCUMENT TYPE: Utility  
FILE SEGMENT: GRANTED  
PRIMARY EXAMINER: Helms, Larry R.  
ASSISTANT EXAMINER: Yu, Misook  
LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP  
NUMBER OF CLAIMS: 23  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)  
LINE COUNT: 2572

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides for new recombinant ribonuclease proteins which are active when expressed by bacteria. This allows the recombinant ribonucleases of this invention to be fused in-frame with ligand binding moieties to form cytotoxic fusion proteins. Furthermore, these proteins are more active than ribonucleases currently available even though the proteins of this invention lack an N-terminal pyroglutamic acid, which has been found to be necessary for ribonucleolytic activity. Because these proteins are recombinant proteins, mutations which increase cytotoxicity can be engineered.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 16 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2005:217226 CAPLUS

DOCUMENT NUMBER: 142:407935

TITLE: Status of RNAs, localized in *Xenopus laevis* oocytes, in the frogs *Rana pipiens* and *Eleutherodactylus coqui*

AUTHOR(S): Nath, Kimberly; Boorech, Jamie L.; Beckham, Yvonne M.; Burns, Mary M.; Elinson, Richard P.

CORPORATE SOURCE: Department of Biological Sciences, Duquesne University, Pittsburgh, PA, 15282, USA

SOURCE: Journal of Experimental Zoology, Part B: Molecular and Developmental Evolution (2005), 304B(1), 28-39  
CODEN: JEZPBS

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Early development in the frog model, *X. laevis*, is governed by RNAs, localized to the vegetal cortex of the oocyte. These RNAs include *Xdazl* RNA, which is involved in primordial germ cell formation, and *VegT* RNA, which specifies the mesoderm and endoderm. To determine whether orthologues of these RNAs are localized and have similar functions in other frogs, we cloned *RpDazl* and *RpVegT* from *R. pipiens*, a frog that is phylogenetically distant from *X. laevis*. RNAs from both genes are localized to the vegetal cortex of the *R. pipiens* oocyte, indicating that the vegetal localization is likely the basal state. The animal location of *EcVegT* RNA in *E. coqui* that we found previously is then a derived state, probably due to the great increase in egg size required for direct development of this species. To answer the question of function, we injected *RpVegT* or *EcVegT* RNAs into *X. laevis* embryos, and assayed animal caps for gene expression. Both of these RNAs induced the expression of endodermal, mesodermal, and organizer genes, showing that the function of *RpVegT* and *EcVegT* as mesoendodermal determinants is conserved in frogs. The RNA localizations and the function of *VegT* orthologues in germ layer specification may be synapomorphies for anuran amphibians.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 28 OF 61 USPATFULL on STN

ACCESSION NUMBER: 2003:145885 USPATFULL

TITLE: Recombinant onconase and chemical conjugates and fusion proteins of recombinant onconase

INVENTOR(S): Goldenberg, David M., Mendham, NJ, UNITED STATES  
Hansen, Hans, Picayune, MS, UNITED STATES  
Leung, Shui-On, Morris Township, NJ, UNITED STATES  
PATENT ASSIGNEE(S): Immunomedics, Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003099629	A1	20030529
APPLICATION INFO.:	US 2002-153882	A1	20020524 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1999-265901, filed on 11 Mar 1999, ABANDONED		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	FOLEY AND LARDNER, SUITE 500, 3000 K STREET NW, WASHINGTON, DC, 20007		
NUMBER OF CLAIMS:	19		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	1 Drawing Page(s)		
LINE COUNT:	941		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Recombinantly-produced Onconase molecules and fusion proteins containing the same are disclosed. The recombinantly-produced Onconase molecule has the sequence of native Onconase, retains the proper folding of native Onconase and has cytotoxic activity similar to that of Onconase purified from oocytes of *Rana pipiens*. cDNA coding for Onconase is extended by one triplet which codes for N-formyl-methionine. When expressed recombinantly, the mutant Onconase has N-formyl-methionine as the N-terminal amino acid, and glutamyl as the penultimate N-terminal residue. Following expression, the N-formyl methionine residue is cleaved and the penultimate glutamyl residues is cyclized to produce Onconase with an N-terminal pyroglutamate residue, and hence the same structure and function as native Onconase.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 30 OF 61 USPATFULL on STN  
ACCESSION NUMBER: 2003:37666 USPATFULL  
TITLE: Recombinant anti-tumor RNase  
INVENTOR(S): Rybak, Susanna M., Frederick, MD, UNITED STATES  
Newton, Dianne L., Rockville, MD, UNITED STATES  
PATENT ASSIGNEE(S): The Department of Health and Human Services National Institutes of Health, Rockville, MD, 20852 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003027311	A1	20030206
APPLICATION INFO.:	US 2001-948391	A1	20010906 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 2001-622613, filed on 31 Jul 2001, PENDING A 371 of International Ser. No. WO 1999-US6641, filed on 26 Mar 1999, UNKNOWN		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-79751P	19980327 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834	
NUMBER OF CLAIMS:	44	
EXEMPLARY CLAIM:	1	
LINE COUNT:	2625	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides for new recombinant ribonuclease proteins which are active when expressed by bacteria. This allows the recombinant

ribonucleases of this invention to be fused in-frame with ligand binding moieties to form cytotoxic fusion proteins. Furthermore, these proteins are more active than ribonucleases currently available even though the proteins of this invention lack an N-terminal pyroglutamic acid, which has been found to be necessary for ribonucleolytic activity. Because these proteins are recombinant proteins, mutations which increase cytotoxicity can be engineered.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 31 OF 61 USPATFULL on STN

ACCESSION NUMBER: 2003:302792 USPATFULL  
 TITLE: Mutant form of cytotoxic ribonucleolytic protein which allows production by recombinant methods  
 INVENTOR(S): Youle, Richard J., Bethesda, MD, United States  
 Vasandani, Veena M., Rockville, MD, United States  
 Wu, Yon-Neng, Bethesda, MD, United States  
 Boix, Ester, Barcelona, SPAIN  
 Ardelt, Wojciech, New City, NY, United States  
 PATENT ASSIGNEE(S): The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6649393	B1	20031118
APPLICATION INFO.:	US 1998-95429		19980610 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1996-626288, filed on 4 Apr 1996		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Nashed, Nashaat T.		
LEGAL REPRESENTATIVE:	Klarquist Sparkman, LLP		
NUMBER OF CLAIMS:	8		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)		
LINE COUNT:	1477		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides recombinant Onc (rOnc) compositions and methods. Recombinant Onc proteins of the invention have an amino terminal methionine and comprise an Onc polypeptide. The amino terminal methionine of the protein allows for recombinant production in a bacterial host cell. Cleaving the amino terminal methionine exposes the amino terminal glutamine of the polypeptide. The Onc polypeptide has an amino terminal glutamine. Cyclization of the amino terminal glutamine of the polypeptide to a pyroglutamyl residue provides rOnc polypeptides and proteins have anti-cancer and anti-viral activity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 32 OF 61 USPATFULL on STN

ACCESSION NUMBER: 2003:302791 USPATFULL  
 TITLE: Mutant form of a cytotoxic ribonucleolytic protein which allows production by recombinant methods  
 INVENTOR(S): Youle, Richard J., Bethesda, MD, United States  
 Vasandani, Veena M., Rockville, MD, United States  
 Wu, Yon-Neng, Bethesda, MD, United States  
 Boix, Ester, Barcelona, SPAIN  
 Ardelt, Wojciech, New City, NY, United States  
 PATENT ASSIGNEE(S): The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)

NUMBER	KIND	DATE
-----		

PATENT INFORMATION: US 6649392 B1 20031118  
APPLICATION INFO.: US 1996-626288 19960404 (8)  
DOCUMENT TYPE: Utility  
FILE SEGMENT: GRANTED  
PRIMARY EXAMINER: Nashed, Nashaat T.  
LEGAL REPRESENTATIVE: Klarquist Sparkman, LLP  
NUMBER OF CLAIMS: 11  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)  
LINE COUNT: 1497

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides recombinant Onc (rOnc) compositions and methods. Recombinant Onc proteins of the invention have an amino terminal methionine and comprise an Onc polypeptide. The amino terminal methionine of the protein allows for recombinant production in a bacterial host cell. Cleaving the amino terminal methionine exposes the amino terminal glutamine of the polypeptide. The Onc polypeptide has an amino terminal glutamine. Cyclization of the amino terminal glutamine of the polypeptide to a pyroglutamyl residue provides rOnc polypeptides and proteins have anti-cancer and anti-viral activity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 37 OF 61 USPATFULL on STN

ACCESSION NUMBER: 2002:181539 USPATFULL  
TITLE: Methods of making nucleic acids encoding ribonucleases  
INVENTOR(S): Saxena, Shailendra K., West Orange, NJ, United States  
PATENT ASSIGNEE(S): Alfacell Corporation, Bloomfield, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6423515	B1	20020723
APPLICATION INFO.:	US 2000-687748		20001014 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1999-394268, filed on 10 Sep 1999, now patented, Pat. No. US 6175003		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Fredman, Jeffrey		
ASSISTANT EXAMINER:	Einsmann, Juliet		
NUMBER OF CLAIMS:	7		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 2 Drawing Page(s)		
LINE COUNT:	329		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB pET11d-rOnc(Q1, M23L) DNA is subjected to two different site-directed mutations, each using an overlapping PCR protocol. One of the site-directed mutations changes the amino acid residue at position 23 of the encoded protein from leucine to methionine, whereby the encoded protein can be made into ranpirnase by cleaving the N-terminal methionine residue and allowing the adjacent glutamine residue to autocyclize. The other site-directed mutation changes the amino acid residue at position 72 of the encoded protein from serine to cysteine, thereby producing an encoded protein that can be made into a cysteinized ranpirnase by cleaving the N-terminal methionine residue and allowing the adjacent glutamine residue to autocyclize.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 40 OF 61 USPATFULL on STN

ACCESSION NUMBER: 2001:8169 USPATFULL  
TITLE: Nucleic acids encoding ribonucleases and methods of making them  
INVENTOR(S): Saxena, Shailendra K., West Orange, NJ, United States  
PATENT ASSIGNEE(S): Alfacell Corporation, Bloomfield, NJ, United States

(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6175003	B1	20010116
APPLICATION INFO.:	US 1999-394268		19990910 (9)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Fredman, Jeffrey		
ASSISTANT EXAMINER:	Einsmann, Juliet C.		
NUMBER OF CLAIMS:	8		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 2 Drawing Page(s)		
LINE COUNT:	249		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB pET1ld-rOnc(Q1, M23L) DNA is subjected to two different site-directed mutations, each using an overlapping PCR protocol. One of the site-directed mutations changes the amino acid residue at position 23 of the encoded protein from leucine to methionine, whereby the encoded protein can be made into ranpirnase by cleaving the N-terminal methionine residue and allowing the adjacent glutamine residue to autocyclize. The other site-directed mutation changes the amino acid residue at position 72 of the encoded protein from serine to cysteine, thereby producing an encoded protein that can be made into a cysteinized ranpirnase by cleaving the N-terminal methionine residue and allowing the adjacent glutamine residue to autocyclize.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 44 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 10

ACCESSION NUMBER: 2000:475689 CAPLUS  
DOCUMENT NUMBER: 133:101138  
TITLE: Purification and sequences of RNase  
-like glycoproteins from Rana pipiens and  
their use in the treatment of tumors  
INVENTOR(S): Ardelt, Wojciech  
PATENT ASSIGNEE(S): Alfacell Corporation, USA  
SOURCE: PCT Int. Appl., 32 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040608	A1	20000713	WO 1999-US30799	19991224
W: JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL				
US 6239257	B1	20010529	US 1998-223118	19981230
EP 1141004	A1	20011010	EP 1999-968949	19991224
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL				
JP 2002534075	T	20021015	JP 2000-592316	19991224
PRIORITY APPLN. INFO.:			US 1998-223118	A 19981230
			WO 1999-US30799	W 19991224

AB Purification and physicochem. properties of four glycoproteins: 2325p4, 2325p4a, 2325p6 and 2728, that are bioactive against human tumor cell lines are disclosed. These glycoproteins are derived from eggs of the Rana pipiens frog, and are members of the superfamily of pancreatic RNases. Each RNase-like glycoprotein from Rana pipiens has (a) an amino acid sequence that is 114 amino acids long, (b) an isoelec. point of .apprx.10, and (c) a mol. weight of .apprx.13,000.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



L5 ANSWER 47 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 11

ACCESSION NUMBER: 2000:472150 CAPLUS

DOCUMENT NUMBER: 133:318111

TITLE: A gender-specific mRNA encoding a cytotoxic ribonuclease contains a 3' UTR of unusual length and structure

AUTHOR(S): Chen, Shin-Lin; Le, Shu-Yun; Newton, Dianne L.; Maizel, Jacob V., Jr.; Rybak, Susanna M.

CORPORATE SOURCE: Laboratory of Biochemical Physiology and Division of Basic Science, SAIC Frederick, National Cancer Institute-Frederick Cancer Research and Development Center, Frederick, MD, 21702, USA

SOURCE: Nucleic Acids Research (2000), 28(12), 2375-2382

CODEN: NARHAD; ISSN: 0305-1048

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A cDNA (2855 nt) encoding a putative cytotoxic RNase (rapLR1) related to the antitumor protein onconase was cloned from a library derived from the liver of gravid female amphibian *Rana pipiens*. The cDNA was mainly comprised (83%) of 3' untranslated region (UTR). Secondary structure anal. predicted two unusual folding regions (UFRs) in the RNA 3' UTR. Two of these regions (711-1442 and 1877-2130 nt) contained remarkable, stalk-like, stem-loop structures greater than 38 and 12 standard deviations more stable than by chance, resp. Secondary structure modeling demonstrated similar structures in the 3' UTRs of other species at low frequencies (0.01-0.3%). The size of the rapLR1 cDNA corresponded to the major hybridizing RNA cross-reactive with a genomic clone encoding onconase (3.6 kb). The transcript was found only in liver mRNA from female frogs. In contrast, immunoreactive onconase protein was detected only in oocytes. Deletion of the 3' UTR facilitated the in vitro translation of the rapLR1 cDNA. Taken together these results suggest that these unusual UFRs may affect mRNA metabolism and/or translation.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 48 OF 61 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 12

ACCESSION NUMBER: 1999:640970 CAPLUS

DOCUMENT NUMBER: 131:283317

TITLE: Recombinant anti-tumor RNase

INVENTOR(S): Rybak, Susanna M.; Newton, Dianne L.

PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA

SOURCE: PCT Int. Appl., 72 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9950398	A2	19991007	WO 1999-US6641	19990326
WO 9950398	A3	19991223		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2324646	A1	19991007	CA 1999-2324646	19990326
CA 2401916	A1	19991007	CA 1999-2401916	19990326
AU 9932074	A	19991018	AU 1999-32074	19990326

AU 755147	B2	20021205		
EP 1068332	A2	20010117	EP 1999-914174	19990326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1277838	A1	20030122	EP 2002-78725	19990326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
US 6869604	B1	20050322	US 2001-622613	20010731
US 2003027311	A1	20030206	US 2001-948391	20010906
US 2003124131	A1	20030703	US 2001-961400	20010925
AU 773347	B2	20040520	AU 2002-18855	20020301
AU 2002018855	A5	20020502		
PRIORITY APPLN. INFO.:			US 1998-79751P	P 19980327
			CA 1999-2324646	A3 19990326
			EP 1999-914174	A3 19990326
			WO 1999-US6641	W 19990326
			US 2001-622613	A3 20010731

AB This invention provides for new recombinant RNase proteins which are active when expressed by bacteria. This allows the recombinant RNases of this invention to be fused in-frame with ligand binding moieties to form cytotoxic fusion proteins. Furthermore, these proteins are more active than RNases currently available even though the proteins of this invention lack an N-terminal pyroglutamic acid, which has been found to be necessary for ribonucleolytic activity. Because these proteins are recombinant proteins, mutations which increase cytotoxicity can be engineered. Thus, the cDNA for the RNase of *Rana pipiens* liver was cloned and sequenced. The enzyme was not recognized by antibodies to Onconase. The cDNA for the liver RNase encoded a signal sequence-containing protein which displayed 4 amino acid changes relative to Onconase. The Q1S mutant of this enzyme was produced with recombinant *Escherichia coli*. This mutant had higher RNase activity than did the corresponding Q1S mutant of Onconase. The *R. catesbeiana* RNase was also prepared with *E. coli*. This enzyme, which contained a normal pyroglutamate N-terminus, was approx.20-fold more active than RNase. *R. pipiens* liver RNase, Q1S *R. pipiens* liver RNase, and *R. catesbeiana* RNase were all more cytotoxic to tumor cells than was Onconase.

L5 ANSWER 53 OF 61 CAPLUS COPYRIGHT 2007 ACS on STM  
 ACCESSION NUMBER: 1997:579829 CAPLUS  
 DOCUMENT NUMBER: 127:257613  
 TITLE: Recombinant ribonuclease proteins and their use for killing tumor cells  
 INVENTOR(S): Rybak, Susanna M.; Newton, Dianne L.; Boque, Lluís; Wlodawer, Alexander  
 PATENT ASSIGNEE(S): Rybak, Susanna M., USA; Newton, Dianne L.; Boque, Lluís; Wlodawer, Alexander; United States Dept. of Health and Human Services  
 SOURCE: PCT Int. Appl., 90 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9731116	A2	19970828	WO 1997-US2588	19970219
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2245804	A1	19970828	CA 1997-2245804	19970219

CA 2245804	C	20070123		
AU 9721306	A	19970910	AU 1997-21306	19970219
AU 726379	B2	20001102		
EP 896625	A2	19990217	EP 1997-906675	19970219
EP 896625	B1	20041103		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

CN 1212016	A	19990324	CN 1997-192442	19970219
NZ 331298	A	20000327	NZ 1997-331298	19970219
JP 2000505300	T	20000509	JP 1997-530289	19970219
JP 3469247	B2	20031125		
AT 281528	T	20041115	AT 1997-906675	19970219
ES 2232860	T3	20050601	ES 1997-906675	19970219
US 6045793	A	20000404	US 1998-875811	19980219

PRIORITY APPLN. INFO.:		US 1996-11800P	P	19960221
		WO 1997-US2588	W	19970219

AB The invention relates to RNases derived from a native RNase found in the oocytes of Rana pipiens. Various humanized and recombinant forms of these mols. are described as well as uses for them. Thus, chimeric RNases were produced with recombinant Escherichia coli. These RNases were shown to inhibit protein synthesis in rabbit reticulocyte lysates and in 4 human tumor cell lines (ACHN, renal carcinoma cells; MDA-MB-231, breast carcinoma cells; SF-539, glioma cells; and HS 578T, breast cancer cells).

=> d his full

(FILE 'HOME' ENTERED AT 12:20:26 ON 09 FEB 2007)

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SEA (RNAS? OR RIBONUCLEAS?) (S)PIPIEN?

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5  FILE BIOTECHABS
5  FILE BIOTECHDS
10 FILE BIOTECHNO
2  FILE CABA
36 FILE CAPLUS
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6  FILE IMSDRUGNEWS
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10 FILE PROMT
1  FILE PROUSDDR
20 FILE SCISEARCH
33 FILE TOXCENTER

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4   FILE USPAT2
5   FILE WPIDS
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6   FILE NLDB
L1  QUE (RNAS? OR RIBONUCLEAS?) (S) PIPIEN?
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    D RANK

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L3  193 SEA L2 (S) (GENE? OR DNA? OR RNA? OR MRNA? OR CDNA? OR POLYNUCLE
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L4  126 SEA L3 (S) (ISOLAT? OR CLON? OR CHARACTER? OR PURIF? OR
    EXPRESS? OR RECOMBINAN?)
L5  61 DUP REM L4 (65 DUPLICATES REMOVED)
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    D IBIB ABS L5 1 2 5 13 16 28 30 31 32 37 40 44 47 48 53

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#### FILE USPATFULL

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 8 Feb 2007 (20070208/PD)  
 FILE LAST UPDATED: 8 Feb 2007 (20070208/ED)  
 HIGHEST GRANTED PATENT NUMBER: US7174569  
 HIGHEST APPLICATION PUBLICATION NUMBER: US2007033695  
 CA INDEXING IS CURRENT THROUGH 8 Feb 2007 (20070208/UPCA)  
 ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 8 Feb 2007 (20070208/PD)  
 REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2006  
 USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2006

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 FILE LAST UPDATED: 8 Feb 2007 (20070208/ED)

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